REMARKS

This Amendment responds to the 16 March 2006 Office Action. Enclosed find a request to extend the time to answer, together with the fee for this request.

The Drawings

The disclosure stands objected to because "there is no description of drawings in the specification." Reconsideration is respectfully requested because the specification at page 13 contains a full page of such description.

The drawings are objected to because they are "unclear and glory." Applicant includes here another copy of the drawings. These drawings are respectfully believed acceptable in clarity and glory because they are copies of the drawings which were accepted by The European Patent Office in the parent PCT application.

The Claims Have Been Amended To
Distinctly Point Out The Claimed Invention

Claims 67 and 70-71 stand rejected "because the terms 'receptor?, NF?B., interferon?" are confusing.

Reconsideration is respectfully requested because the claims do not use these terms. Claim 67 uses the term "activated receptor ?" and claim 70 uses the term "interferon ?"; the ? symbol used is the Greek letter gamma. Claim 71 uses the

phrase "effective to inhibit NF?B" the ? symbol is the Greek letter kappa. If these fonts fail to display properly on the Examiner's computer, the Examiner might want to assure that the Examiner's Adobe Acrobat® Reader software contains an up-to-date set of fonts.

Claims 53-73 stand rejected because the term "5,ha" is vague and unclear.

The application illustrates the claimed compound as having the structure illustrated here. The correct chemical name for this compound is 3-[2-[decahydro-6-hydroxy-5-(hydroxy-methyl)-5,8a-dimethyl-2-methylen-1-napthalenyl]ethylidene] di-hydro-4-hydroxy-2(3h)-furanone. The Examiner correctly recognizes that the claims include a typographical error in this name, saying "5,ha" rather than "5,8a." The claims are here amended to correct this typographical error.

The OFFICE ACTION Fails To State A *Prima Facie* Case Of Failure To Provide An Enabling Disclosure

Claims 53 to 73 stand rejected because "the specification does not enable the instant compound to alter the gene expression and therefore to treat any and all known or unknown diseases." *See* OFFICE ACTION at 6, 11, 14, 18, 22. Reconsideration is requested because the claims neither require "altering gene expression," nor purport to cover "any and all known or unknown diseases."

The OFFICE ACTION (at pages 8, 10, 12) says that "[t]he instant invention is drawn to a method of diagnosing a patient." The OFFICE ACTION then rejects various claims because "Applicant has not provided written description on how to diagnose a patient with any and all possible diseases known. *See* OFFICE ACTION at 5.

Reconsideration is requested because the claims are not drawn to "a method of diagnosing a patient." To the contrary, the claims are drawn to a method of treating a patient. Further, the claims do not purport to cover "any and all known or unknown diseases."

The OFFICE ACTION says that diagnostic methods are known in the prior art. For example, the OFFICE ACTION says that how to diagnose Alzheimer's Disease and autoimmune diseases is known in the art. *See* OFFICE ACTION at 8, *citing* Luciano SASO *et al.*, *Abnormal Glycosylation of a_2–Macroglobulin, a Non-Acute-Phase Protein, In Patients with Autoimmune Diseases*, 17 INFLAMMATION 465 (1993). Similarly, the OFFICE ACTION says that how to diagnose autoimmune diseases and AIDS is known in the art. *See* OFFICE ACTION at 20 ("In addition, … arthritis septicemia, autoimmune diseases, … AIDS, etc. can be diagnosed by methods comprising determining from a sample … an abnormally decreased or increased level of TR6 polypeptide or TR6 mRNA."). Similarly, the OFFICE ACTION

provides evidence showing that how to diagnose Syndrome X (or "metabolic syndrome," as it is now called) is known in the art. *See* Altan ONAT *et al.*, *Metabolic Syndrome: Major Impact on Coronary Risk...*, 165 ATHEROSCLEROSIS 285, 286 (2002) (Syndrome X is diagnosed "when three of more of the following five risk determinants were present: waist circumference (men > 102 cm, women > 88 cm), triglycerides > 150 mg/dl, HDL-C (men < 40, women < 50 mg/dl), blood pressure (> 130/ > 85 mmHg), and fasting glucose > 110 mg/dl."). Because diagnostic methods are known in the art, Applicant need not provide an enabling disclosure of them.

The OFFICE ACTION (at page 5) alleges that "there is no way to positively identify a person with Alzheimer's without direct examination of the barain." Withdraw of this factual allegation is required because it lacks evidentiary support in the record of this proceeding. Further, the Patent Office's own records contradict it. *See e.g.,* Stanley APPEL, *Diagnosis of Alzheimer Disease*, United States Letters Patent No. 4,701,407 (1987); Boyd E. HALEY, *Detection of Alzheimer's Disease*, United States Letters Patent No. 5,445,937 (1995); and William E. KLUNK *et al., Compound for the Antemortem Diagnosis of Alzheimer's Disease*, United States Letters Patent No.6,114,175 (2000).

The OFFICE ACTION (at page 20) says that autoimmune disease, syndrome, and Alzheimer's Disease can be treated with TR6 polypeptides, poly-

nucleotides and recombinant materials. The OFFICE ACTION then argues that because these therapeutic regimens are already known "the existence of these obstacles establishes that the contemporary knowledge of the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face."

Reconsideration is requested, because the existence of other therapeutic regimens in the prior art *encourages* – not *prevents* – one of skill in the art from accepting a therapeutic regimen.

Regarding claim 73, the OFFICE ACTION asks, "Do they enable this plant everywhere in the planet to treat Syndrome X? Does this plant under any and all condition can treat Syndrome X? This is a scope of enablement rejection." *See* OFFICE ACTION at 3.

Reconsideration is respectfully requested because this is not a "scope of enablement rejection." Rather, it is a pair of apparently rhetorical questions. This pair of questions fails to state the *prima facie* factual basis required to maintain an enablement rejection.

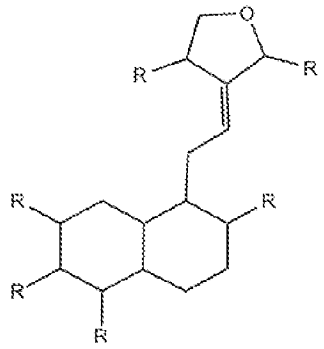
Various claims stand rejected because one of skill in the art would need to do "undue experimentation" to screen and determine which of the claimed "compounds" would be therapeutically useful. *See e.g.,* OFFICE ACTION at 25. Reconsideration is respectfully requested, because Applicant has already done this

screening, and accordingly claims one and only one compound. No further "screening" is necessary.

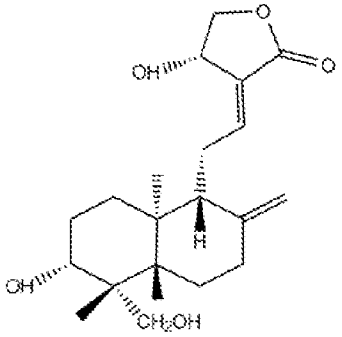
The OFFICE ACTION Fails To State A *Prima Facie* Case Of Anticipation Or Obviousness

Various claims stand rejected as anticipated over John G. BABISH *et al.*, WO/96/17605 (1996); John G. BABISH *et al.*, U.S. Patent Publication No. 2002/0068098 (2002); Srinivas NANDURI *et al.*, U.S. Patent Publication No. 2002/0016324 (2002); Srinivas NANDURI *et al.*, U.S. Patent No. 6,410,590 (2002); Srinivas NANDURI *et al.*, U.S. Patent No. 6,486,196 (2002); Geoffrey D. WHEELOCK *et al.*, U.S. Patent No. 5,833,994 (1998); and Geoffrey D. WHEELOCK *et al.*, WO 98/30213 (1998).

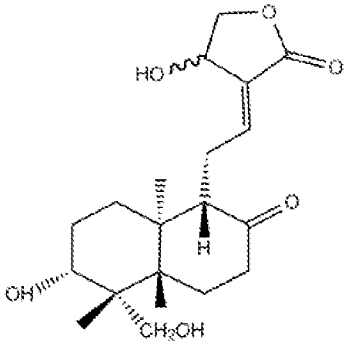
Reconsideration is requested because the art of record fails to teach the claimed compound. The claims require not "andrographolide" (as taught by BABISH *et al.*, U.S. '098); rather, the claims cover 3-[2-[decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-naphthalenyl]ethylidene]-dihydro-4-hydroxy-2(3h)-furanone. This compound is not taught by any reference of record. This is illustrated in the accompanying Figure:



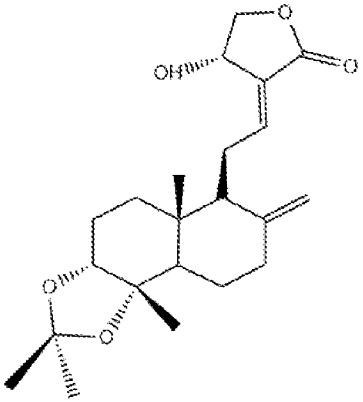
John G. BABISH *et al.*, WO '605



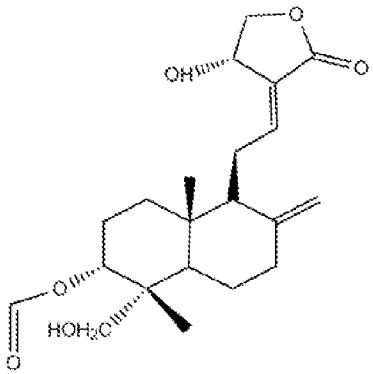
The claimed compound



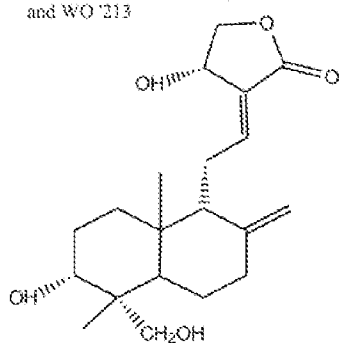
John G. BABISH *et al.*, U.S. '098
G.D. WHEELOCK *et al.*, U.S. '994; U.S. '063 and WO '213



NANDURI *et al.*, U.S. '324



NANDURI *et al.*, U.S. '196



NANDURI *et al.*, U.S. '590

For example, BABISH *et al.*, WO '605 and NANDURI *et al.*, U.S. '324, U.S. '590, and U.S. '196 (2002) fail to teach methylation at C4. Similarly, BABISH *et al.* U.S. '098, and WHEELOCK *et al.*, U.S. '994, U.S. '063 and WO '213 fail to teach oxidation at C9. No art of record teaches the claimed compound.

Similarly, the claims are drawn to methods to treat AIDS, Syndrome X, non-autoimmune Alzheimer's Disease, and autoimmune disease. In contrast, the art of record teaches different therapeutic uses.

BABISH *et al.*, U.S. '098 and U.S. '350 teaches the use of andrographolide as a diterpene triepoxide lactone or triptolide adjunct.

BOGGS *et al.*, U.S. '269 teaches use as an antibiotic adjunct. Applicant respectfully disagrees with the Examiner's factual assertion that "bacterial infection is broadly encompassed by AIDS" because AIDS does not encompass bacterial infection. AIDS is caused by an infection by a retrovirus, not a bacterium. The two different classes of infection require two completely different therapies. For example, AIDS is treated by anti-retroviral drugs, while bacterial infection is treated by antibiotics. Further, anti-retroviral drugs are structurally dissimilar from antibiotics. Further, no anti-viral drug has been shown effective against bacterial infection, and no antibiotic has been shown effective against AIDS.

NANDURI *et al.*, U.S. '196, teaches that andrographolide-containing preparations "have been assayed for the ability to decrease the expression and phosphorylation of $p34^{cdc2}$ kinase, cyclin B and c-Moss for treating or preventing pathogenicity." NANDURI '196, however, fails to teach *the results* of those assays (that is, he fails to say whether or not the assays show any effect); NANDURI '196 therefore provides a mere "invitation to experiment," not an enabling prior art disclosure of the claimed uses.

PANOSSIAN *et al.*, teaches to use andrographolide for "*in vitro* effect on the activation and proliferation of immunocompetent cells." In contrast, autoimmune disease is thought to be caused by an overly-active immune system. Therefore, by teaching that andrographolide *activates* the immune system, PANOSSIAN teaches away from the use of the claimed compound to treat autoimmune diseases.

WHEELOCK *et al.*, WO '213 teaches oncology and tumor treatment. WHEELOCK *et al.*, U.S. '994, teaches anal tumor treatment. WHEELOCK *et al.*, U.S. '063 is simply a Divisional application of the '994 application; as such, it teaches the same thing.

Further, the Examiner concedes that the predictability in the pharmaceutical art is low, because minor structural differences can precipitate major changes in toxicology or clinical efficacy. This shows that it would not have been obvious to modify any of the prior art compounds to *make* the claimed compound, and that it would not have been obvious to *use* such a modified compound for the claimed uses.

Applicant Respectfully Requests Reconsideration

Applicant respectfully believes that the application is in condition for prompt allowance. Applicant accordingly respectfully requests withdraw of all rejections and allowance of the claims.

Respectfully submitted on behalf of Applicant by its attorneys,
PHARMACEUTICAL PATENT ATTORNEYS, LLC

/s/

Mark Pohl, Reg. No. 35,325
Mark.Pohl@LicensingLaw.Net
☎ +1 (973) 984-0076

Pharmaceutical Patent Attorneys LLC
55 Madison Avenue, 4th floor (P 4014)
Morristown, NJ 07960-6397 USA
19 June 2006

enclosures

Replacement drawings

SD:\HP Ingredients\10.xxx,xxx – Amendment - Preliminary.doc